


Review Article

| | | | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|------------------------------------------------------------------------------------|----------------------------|
| Pig Erysipelas — A Review | |  | Veterinary Medicine |
| Keywords: swine, erysipelas, zoonotic agent, public health. | | | |
| Arlind Stafa | | Agricultural University of Tirana, Faculty of Veterinary Medicine | |
| Keti Margariti | | Agricultural University of Tirana, Department of Animal Production | |
| Ilirian Kumbe | | Agricultural University of Tirana, Faculty of Veterinary Medicine | |
| Abstract | | | |
| <p>Swine erysipelas is an important bacterial disease of pigs caused by infection with <i>Erysipelothrix rhusiopathiae</i>; the clinical and pathological features of the disease have been well-described. Infection with <i>Erysipelothrix rhusiopathiae</i> has a significant economic impact on pig production systems worldwide. The organism has the ability to persist for long periods in the environment and survive in marine locations. Infection in man is occupationally related, occurring principally as a result of contact with animals, their products or wastes. <i>Erysipelothrix rhusiopathiae</i> is a causative agent zoonotic and it affectet people. At highest risk are butchers, abattoir workers, veterinarians, farmers, fisherman, fish handlers, and housewives. In addition to others, swine erysipelas, when uncontrolled, is an economically significant disease Stages Capable of affecting all of pork production. Therefore, the impact of this infection has been both in economic losses and public health.</p> | | | |

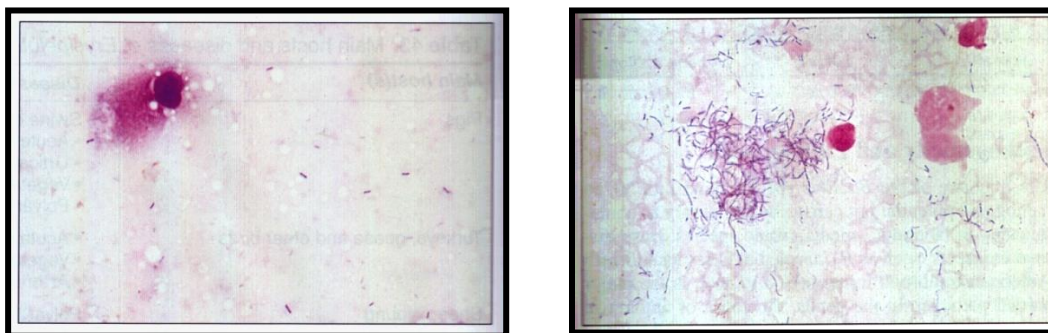
Introduction

Swine erysipelas is an important bacterial disease of pigs caused by infection with *Erysipelothrix rhusiopathiae*; the clinical and pathological features of the disease have been well-described (Wood and Henderson, 2006 Eric J. Neumann et al 2009). Swine erysipelas found in literature in different languages such as Schweinerotlauf, Vlekziekte, Rouget du porc, Mal Rossino, erysipelas del cerdo, etc. The causative organism of swine erysipelas, *Erysipelothrix rhusiopathiae*, was first isolated from a pig in 1882 by Louis Pasteur. In 1885, *E. rhusiopathiae* was isolated from pigs in the United States (Smith 1885). Until the last years of the XIX century, this disease was not studied so confused with the Antrax. In 1882-1883 Thyillier and Pasteur describes the organism, isolated from pigs by the name "Rogue". Leoffleri in 1883-1886 studied and published the first complete description about the cause of swine erysipelas, and presented the clinical signs of disease. Paster, Konjev, Kitt, Visheleveskij and many other authors, worked out ways of protecting pigs from erysipelas, preparing biological preparations, vaccines and serums. For the first 40 years after its initial recognition, swine erysipelas was reported to occur sporadically in the swine population. For the first time in Albania swine erysipelas was diagnosed in 1936. Despite continuous immunizations against swine erysipelas in Albania has continuously outbreaks of swine erysipelas. Swine erysipelas, when uncontrolled, is an economically significant disease capable of affecting all stages of pork production. The greatest losses usually manifest as cases of sudden death or acute septicemia in grow–finish pigs.

The sequel of surviving an acute infection is often chronic lameness and arthritis, resulting in poor growth. Both erysipelas-associated septicemia and arthritis are responsible for significant production losses and decreased carcass value.

Etiology

Causative agent of swine erysipelas is *Erysipelothrix rhusiopathiae*. In 1876 *Erysipelothrix muriseptica* was isolated from the blood of a mouse with septicemia by Koch. In 1966, the name was changed to *E. rhusiopathiae*. The genus *Erysipelothrix* is now subdivided into two major species, *E. rhusiopathiae* (Migula 1900; Skerman et al. 1980) and *Erysipelothrix tonsillarum* (Takahashi et al. 1987). In addition, there are other strains that constitute one or more additional species currently known as *Erysipelothrix* sp.-1 (Takahashi et al. 1992, 2008), *Erysipelothrix* sp.-2 (Takahashi et al. 1992, 2008), *Erysipelothrix inopinata* (Verbarg et al. 2004), and *Erysipelothrix* sp.-3 (Takahashi et al. 2008). *Erysipelothrix* spp. strains can be differentiated by precipitation reactions using hyperimmune rabbit antiserum into at least 28 serotypes (Kucsera 1973; Wood and Harrington 1978). Field cases of swine erysipelas throughout the world are predominantly caused by *E. rhusiopathiae* serotypes 1a, 1b, or 2, while less common serotypes of *E. rhusiopathiae* typically have lower virulence for swine. The organism is presented in the form of rods, straight, angled, in the form of the letter "V" or "X" or spiral with 0.2-0.4 x 0.8-2.5 μ . *Erysipelothrix* spp. is a gram positive microorganism *Erysipelothrix* are nonmotile, nonsporulating, non-acid-fast, slender gram-positive rods (Brooke and Riley 1999). All the members of the genus are facultative anaerobes and grow between 5°C and 44°C, with optimal growth occurring between 30°C and 37°C (Brooke and Riley 1999; Carter 1990; Sneath et al. 1951).



Microscopic view of *Erysipelothrix rhusiopathiae* (the method of Gram coloration)

In solid media, colonies are clear, circular, and very small (0.1–0.5 mm in diameter), after 24 hours of incubation at 35°C or 27°C (Carter 1990). Most strains induce a zone of partial hemolysis on blood agar media, usually with a green color. The members of genus *Erysipelothrix* are generally inactive and does not react with catalase, oxidase, methyl red, or indole (Cottral 1978). They produce acid and hydrogen sulfide in triple-sugar iron agar (Vickers and Bierer 1958; White and Shuman 1961).

Epidemiology

Erysipelothrix rhusiopathiae is worldwide in distribution and is ubiquitous. The most important reservoir of *E. rhusiopathiae* is domestic pig. It is estimated that 30-50% of healthy pigs harbor this organism in their tonsils and other tissues linfoide. Pigs infected with *E. rhusiopathiae* can excrete the bacteria in feces or nasal secretions constituting an important source of infection. Pigs affected by acute form of the disease shed with abundance *E. rhusiopathiae* in faeces, urine, saliva and nasal secretions. So, the soil, the floor of the stables, food and drinking water contaminated by infected pigs can serve as a route for indirect transmission of infection. In addition they are reported contamination of surface and soil water from infected rodent and sewage derived from meat conservation factories. Notably potential reservoirs include: sheep, cattle, horses, dogs, mice, rats, fresh and saltwater fish, marine mammals, turkeys, chickens, ducks, geese, sparrows, starlings, and blackbirds). Survival of *Erysipelothrix* spp. in soil is less than 35 days (Wood 1973). *Erysipelothrix* spp. can be inactivated by commonly available disinfectants.

Public health

Swine erysipelas is a zoonotic disease. At highest risk are butchers, abattoir workers, veterinarians, farmers, fisherman, fish handlers, and housewives (Reboli and Farrar 1989). The most common form of the disease manifests in humans as an acute localized painful cellulitis with reddening of the skin known as “erysipeloid” (Rosenbach 1909). Historically, “erysipeloid” has been known by such names as whale finger, seal finger, speck finger, blubber finger, fish poisoning, fish handler’s disease, and pork finger.



Fig. 1. "Erysipeloid" infection in fingers and hands

Rarely, *E. rhusiopathiae* causes septicemia, often resulting in endocarditis that is frequently fatal.

Pathogenesis

Research using pigs free from microorganisms (microbiologically sterile) have shown that *E. rhusiopathiae* is the only causative agent of erysipelas in pigs and does not require the presence of other microorganisms, causing various infections, to cause erysipelas. There are marked differences in virulence between strains of *E. rhusiopathiae*, modulated by virulence factors that are partially characterized and have been recently reviewed (Wang et al. 2010). Most important are neuraminidase, capsular polysaccharides, and surface proteins. Neuraminidase is an enzyme that cleaves sialic acids from glycoproteins, glycolipids, and polysaccharides on host cell walls, providing bacterial nutrients and aiding in bacterial adhesion and tissue invasion (Nakato et al. 1986, 1987; Schauer 1985). The polysaccharide capsule of *E. rhusiopathiae* is important in resistance to phagocytosis by host cells (Shimaji et al. 1994).

Route of exposure to *E. rhusiopathiae* in pigs is primarily oral with initial infection of the tonsils or gastrointestinal mucosa. (Jeffrey J. Zimmerman et al. 2012). It was found that pigs less than 3 months of age (due to a protective effect of passively acquired immunity) or pigs older than 3 years of age (due to repeated subclinical disease) are generally least predisposed to erysipelas (Jeffrey J. Zimmerman et al. 2012). Bacteria may also enter through skin abrasions by direct contact or by bites of arthropods that can serve as mechanical vectors (Chirico et al. 2003).

Usually, bacteremia develops within 24 hours in the absence of an effective immune response. Subsequent septicemia results in distribution of the organism throughout the body. According to Schulz et al. (1975b, 1977), early pathogenesis of systemic phase consists of changes that include capillaries and venules of most body organs, including the synovial tissue. This process is described as a coagulopathy generalized shock, who within 4 days followed by a thrombosis of fibrin, diapedesis, vascular endothelium invasion by bacteria, and fibrin deposition in the perivascular tissue. In acute forms of swine erysipelas, hemolysis frequently observed. May also occur perivascular tissue systemic necrosis, caused by the interaction with the microcirculation.

Dromer et al (1970) observed a high incidence of acute encephalomalacia form caused experimentally and hypothesised that some strains of the organism are endotheliotropic and damage endothelial cell barrier in the central nervous system (CNS). It can be caused a weak response of delayed hypersensitivity to *E. rhusiopathiae* and transferred via lymphocytes. Information about the pathogenesis of chronic form erysipelas first derived from studies on the development of arthritic lesions, which have prompted interest because of the apparent similarity with lesions that occur during human rheumatoid arthritis. Based on observations of Schulz et al. (1975, 1977), in the form of chronic articular lesions start with an acute synovitis can occur in less than 3-10 days after exposure to *E. rhusiopathiae*.

Eventually, there is connective tissue activation in predisposed sites of infection, including joints, heart valves, and skin (Schulz et al. 1976b). Sequestration of *E. rhusiopathiae* in the cytoplasm of chondrocytes of articular cartilage is reported (Franz et al. 1995), and likely provides protection from host immunity, contributing to chronic arthritis. There is no experimental evidence that susceptibility to swine erysipelas is related to the genetics of the host. Sudden changes in weather, especially hot summer weather, or other stressors have been implicated in increased incidence of disease (Jeffrey J. Zimmerman et al. 2012)

Clinical signs

They are described three clinical forms of swine erysipelas, acute, subacute, and chronic.

Acute form

The acute form is septicemic disease. This form is characterized by sudden outbreaks, sometimes with unexpected death of one or more animals. In addition to others, this form manifests as a sudden onset of any combination of the following: acute death; abortions; depression; lethargy; pyrexia 40–42°C or greater, withdrawal, lying down, painful joints evidenced by stiff, stilted gait, reluctance to move and/or vocalization during movement; partial or complete inappetence; and characteristic pink, red, or purple raised firm rhomboid or squared “diamond skin” lesions (.....). Some pigs may appear normal and have rectal temperature around 41° C. In nonfatal cases, the skin lesions will gradually disappear within 4–7 days. In pigs that survive rectal temperature can be return to normal within 5–7 days. Skin lesions (as diamond skin) occur earlier, about 2 or 3 days after exposure to swine to the *E. rhusiopathiae*. In the acute fatal form, appear on the skin cyanotic colored area in the abdomen, ears, tail, on the inner surface of the thigh and on jaw.

Subacute form

The subacute form is also septicemic but is clinically less severe than the acute form. In this form of the disease shown clinical signs that are less pronounced than those held in the acute form. Animals do not appear very sick; temperature cannot be high or persist for a long period of time; appetite can be not affected; shown a little skin lesions, which can be seen with difficulty; if sick animals are visible, do not remain in this state for as long a time as when affected by acute forms of erysipelas. Some cases of subacute form appear so weak that it can remain invisible.



Fig. 2. Rhomboid skin lesions in a pig infected with *Erysipelothrix rhusiopathiae*.

Chronic form

Acute or subacute form of the disease or subclinical infection, can pass on chronic form, which is generally characterized by signs of arthritis. The most economically significant form is chronic arthritis that may appear as soon as 3 weeks after the initial outbreak. Sometimes it may shown signs of cardiac insufficiency and may have difficulty in movements that are visible, also accidentally causing sudden death. Chronic polyarthritis appears in joints, which shows varying degrees of swelling, sometimes in less than 3 weeks after infection. Affected animals are mildly to markedly lame with associated reduction in feed intake. A second manifestation of chronic erysipelas is vegetative valvular endocarditis, which may lead to cardiac insufficiency and consequent pulmonary edema and respiratory signs, lethargy, cyanosis, or sudden death.

Lesions

Macroscopic lesions

Lesions rhomboid (diamond skin) are features of acute form of swine erysipelas and when displaying generalized represent a reliable indicator of septicemia. These lesions are pathognomonic for swine erysipelas. In pigs died from the acute form, it is often very visible presence of diffuse cutaneous hemostasis, especially around the snout, ears, jowls, throat, abdomen, and thighs. It may have congestion of the lungs and they appear edematous. In addition to skin lesions, other lesions typical of septicemia are observed, including enlarged and congested lymph nodes and enlarged spleen. Petechiae and ecchymoses may be found in the renal corte, heart (epicardium and atrial myocardium), and occasionally elsewhere. Joints may be slightly enlarged and the synovium and periarticular tissues are typically distended by serofibrinous exudates that may also fill the joint cavity (Jeffrey J. Zimmerman et al. 2012).

Valvular endocarditis can be seen as proliferative, granular growth on the heart valves (mitral valve most common).

Microscopic lesions

Microscopic lesions in acute erysipelas are predominantly in blood vessels, resulting in associated ischemia and necrosis. A microscopic examination of skin lesions reveals damage capillaries and venules, with perivascular infiltration of lymphocytes and fibroblasts. Vascular lesions can be seen in the heart, kidneys, lungs, liver, nervous system, skeletal muscles, and synovial membranes. Accidentally hemorrhagic nephritis can be seen with inflammatory changes. Are described lesions in the central nervous system consisting of the permeability angiopathy changes, degeneration of neurons, swelling of endothelial cells, and malacic foci in the brain, neural trunk, and spinal cord. Are described lesions in the central nervous system consisting angiopathy changes in permeability of blood vessels, degeneration of neurons, swelling of endothelial cells, and foci of malacia in the brain, nerves, and spinal cord.

Diagnosis

For diagnosis of *Erysipelothrix* spp. a variety of tests are available. It can be isolated *Erysipelothrix* spp from blood or fluids 24-48 hours after initiation of disease. To diagnose swine erysipelas, are used more serological tests.

We can use on the slide agglutination, tube, passive haemagglutination, complement fixation, ELISA and indirect immunofluorescence, immunohistochemistry, conventional PCR and Real-time PCR.

Immunity

Both humoral and cell-mediated immunity play a role in host defense against *E. rhusiopathiae* infection. A significant role of humoral immunity is implied since therapy with antiserum has been widely used as an effective treatment for acute septicemia. (Jeffrey J. Zimmerman et al. 2012). Shimoji et al. (1994, 1996) demonstrated that *E. rhusiopathiae* bacteria opsonized with immune serum are readily eliminated by neutrophils, peripheral mononuclear cells, or macrophages in contrast to nonopsonized bacteria. This suggests that the protective activity of antiserum is mediated by the opsonic activity of immunoglobulin G (IgG) antibodies in type I phagocytosis (Shimoji 2000), and that participating antigens are on the bacterial cell surface.

The role of cellular immunity in protection is less clear. Studies in which mice were immunized with acapsular *E. rhusiopathiae* YS-1 strain demonstrated protective antibodies as well as a cell-mediated response evidenced by significant proliferation in spleen cells harvested on 7, 15, and 21 days postimmunization in response to *E. rhusiopathiae* antigen (Shimoji et al. 1998b).

The relative contribution of cell-mediated immunity to protection and the bacterial antigens involved in inducing cell-mediated immunity is unknown (Jeffrey J. Zimmerman et al. 2012).

Treatment

Treatment of swine erysipelas with hiperimun serum originating from horses, was introduced in 1899. 50 years later it was used antibiotics, but until then the administration of antiserum was the only treatment available. The preferred treatment to the *Erysipelothrix* spp. is done by administration of penicillin. It is known that this organism is very sensitive to penicillin and early treatment in an outbreak of acute disease generally results in a rapid response within 24-36 hours. However, most strains are also susceptible to ampicillin, cloxacillin, benzylpenicillin, ceftiofur, tylosin, enrofloxacin, and danofloxacin (Yamamoto et al. 2001).

Specific Prophylaxis

Prevention of swine erysipelas is best accomplished by immunization programs. Current vaccines are based on *E. rhusiopathiae* serotypes 1 or 2 and are either inactivated bacterins for intramuscular injection or attenuated (avirulent live) vaccines designed for whole herd mass treatment via drinking water (Jeffrey J. Zimmerman. 2012) Most bacterins are serotype 2 (Eamens et al. 2006; Wood 1979) and most attenuated live vaccines contain serotype 1a isolates (Opriessnig et al. 2004).

References

1. Brooke CJ, Riley TV. 1999. J Med Microbiol 48:789–799.
2. Carter GR. 1990. *Erysipelothrix rhusiopathiae*. In JR Cole, ed. Diagnostic Procedures in Veterinary Microbiology and Mycology, 5th ed. Springfield, IL: Academic Press, pp. 195–196.
3. Cottral GE. 1978. *Erysipelothrix*. In Manual of Standardized Methods for Veterinary Microbiology. Ithaca, NY: Cornell University Press, pp. 429–436, 671, 672, 679, 687.
4. Eamens GJ, Chin JC, Turner B, Barchia I. 2006. Vet Microbiol 116: 138–148.
5. Eric J Neumann et al. Safety of a live attenuated *Erysipelothrix rhusiopathiae* vaccine for swine. Veterinary Microbiology 135 (2009) 297–303.
6. Jeffrey J. Zimmerman et al. 2012. Swine diseases 10th edition, p 750-760
7. Kucsera G. 1973. Int J Syst Bacteriol 23:184–188.
8. Migula W. 1900. System der Bakterien, Vol. 2. Jena, Germany: Gustav Fischer.
9. Nakato H, Shinomiya K, Mikawa H. 1986. Pathol Res Pract 181: 311–319. 1987. Pathol Res Pract 182:255–260.
10. Opriessnig T, Bender JS, Halbur PG. 2010. J Vet Diagn Invest 22:86–90.
11. Rosenbach PJ. 1909. Z Hyg Infektionskr 63:343–369.
12. Reboli AC, Farrar WE. 1989. Clin Microbiol Rev 2:354–359.

13. Schulz LC, Drommer W, Seidler D, et al. 1975a. Beitr Pathol 154:27–51. -- 1975b. Beitr Pathol 154:1–26.
14. Skerman VBD, McGowan V, Sneath PHA. 1980. Int J Syst Bacteriol 30:225–420.
15. Smith T. 1885. Second Annual Report of the Bureau of Animal Industry. Washington. D.C.: USDA, p. 187.
16. Sneath PH, Abbott JD, Cunliffe AC. 1951. Br Med J 2: 1063–1066.
17. Takahashi T, Fujisawa T, Tamura Y, et al. 1992. Int J Syst Bacteriol 42:469–473.
18. Verbarg S, Rheims H, Emus S, et al. 2004. Int J Syst Evol Microbiol 54:221–225.
19. Wood R L, Henderson L M, 2006. Erysipelas. In: Straw B. E, Zimmerman, J J D'Allaire, S, Taylor D J. (Eds.), Diseases of Swine. Blackwell Publishing Professional, Ames, Iowa, USA, pp. 629–638.
20. Wood RL, Harrington R Jr. 1978. Am J Vet Res 39:1833–1840.
21. White TG, Shuman RD. 1961. J Bacteriol 82:595–599.
22. Wang Q, Chang BJ, Riley TV. 2010. Vet Microbiol 140:405–417. White TG, Shuman RD. 1961. J Bacteriol 82:595–599.
23. Shimoji Y, Mori Y, Hyakutake K, et al. 1998a. J Clin Microbiol 36: 86–89.
24. Yamamoto K, Kijima M, Yoshimura H, Takahashi T. 2001. J Vet Med B Infect Dis Vet Public Health 48:115–126.